Prostate embryology, anatomy and physiology

Embryology

5 paired epithelial buds project posteriorly from urethra into USM at 13-16 weeks under the influence of DHT

Top pairs derived from mesoderm – form TZ/periurethral zones

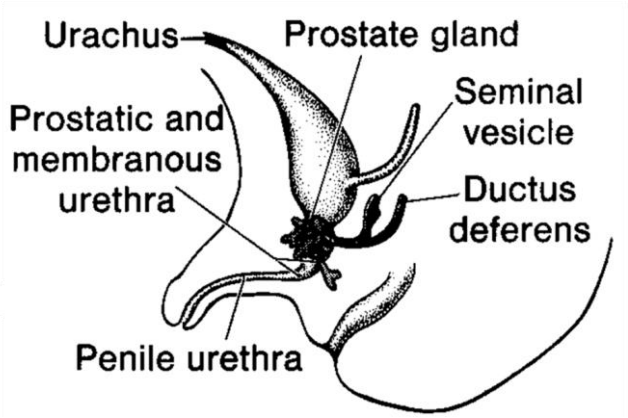
- Low secretory activity
- Apoptosis

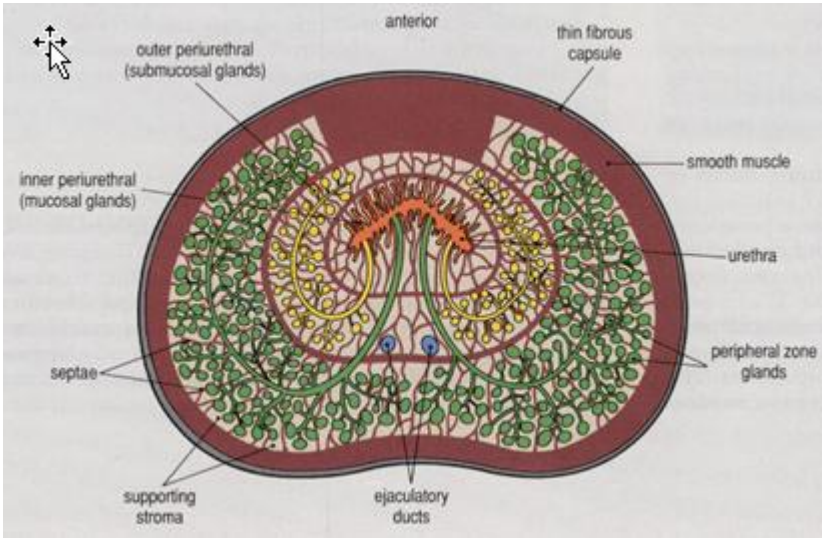
Lower pairs derived from endoderm – PZ

Outer duct - high mitosis, low secretion

Mid duct – less mitosis, high secretion

Inner duct – no mitosis, no secretion, apoptosis





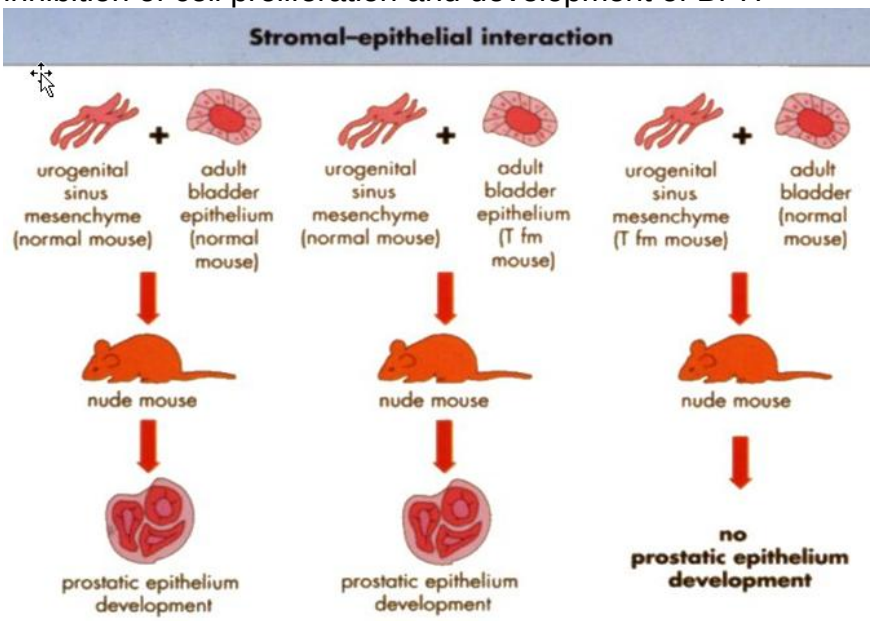
<u>Stromal-epithelial interaction</u>

Prostate development requires presence of surrounding stroma

Determined by classic work by Jerry Cunha 1983

- Urogenital sinus mesenchyme (USM) induces prostate epithelial differentiation from adult bladder epithelium
- Absolute requirement for USM androgen receptor (not present in testicular feminisation)

Further growth of prostatic epithelium regulated by interaction with basement membrane and stromal cells - ? defect in stromal component responsible for inhibition of cell proliferation and development of BPH

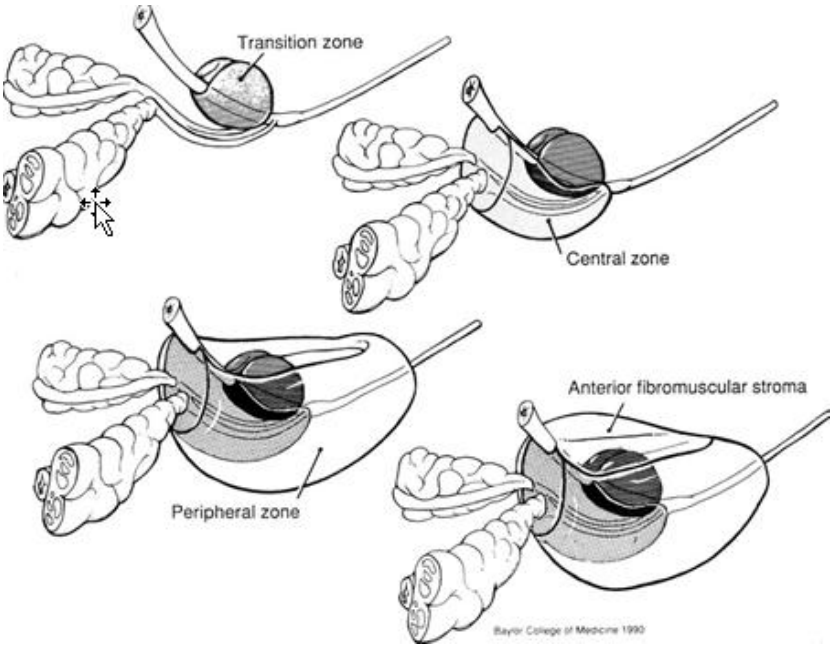


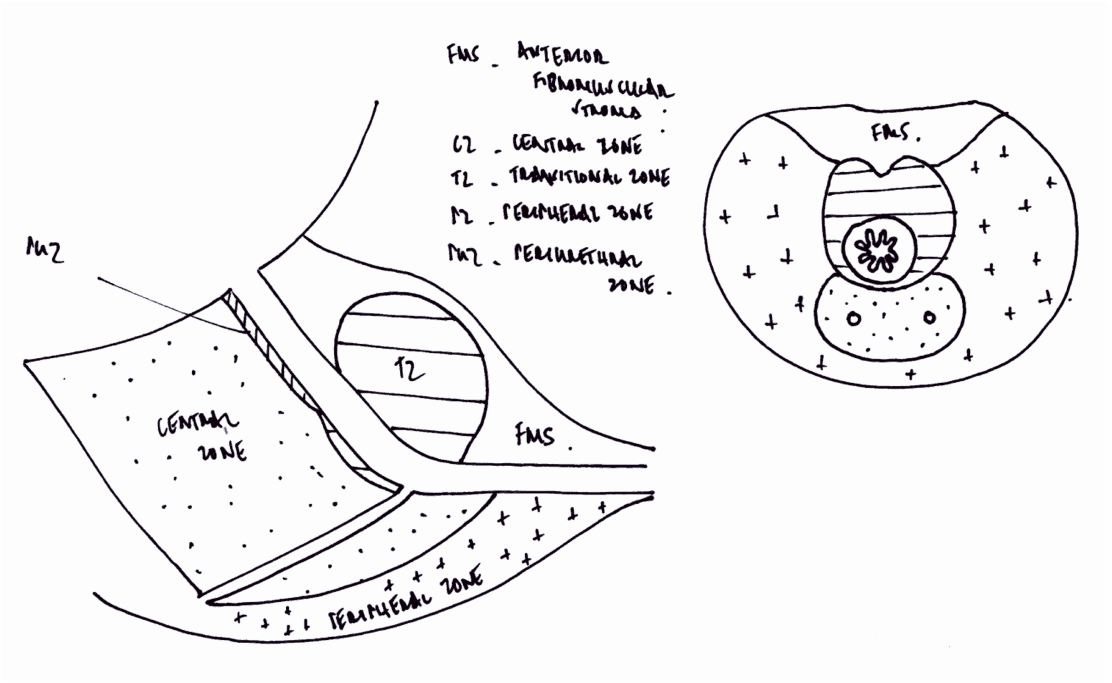
Anatomy

70% glandular (simple columnar or cuboidal epithelium); 30% fibromuscular stroma. Glandular elements:

70%	peripheral zone		(70% cancers)
25%	central zone		(5-10% cancers)
5-10%	transitional zone	lateral lobes	(20% cancers)
1%	periurethral zone	middle lobe	

NB. urethral angle (typically 35') divides periurethral zone from TZ (see below)
Central zone - Wolffian structures – under influence of T
Remaining prostate – urogenital sinus mesenchyme – under influence of DHT





<u>Pre-prostatic sphincter</u>

Signet ring, deficient posteriorly (remember anterior fibromuscular stroma)

Innervation of sphincter predominantly adrenergic and chlolinergic, with others (NANC):

Cholinergic
- epithelial secretion

Adrenergic
- 98% in stroma, not epithelium
- 90% α1 (60% α1a)
- 10% α2
- smooth muscle contraction

Neuroendocrine cells
- Serotonin, calcitonin, TSH, somatostatin
- regulation of secretion & cell growth

NANC
- Substance P, neuropeptide Y, encephalins, VIP
- Function unknown

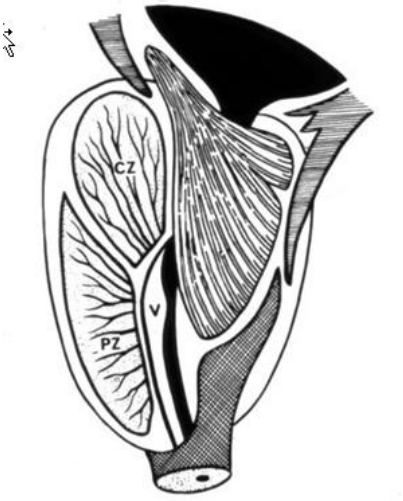
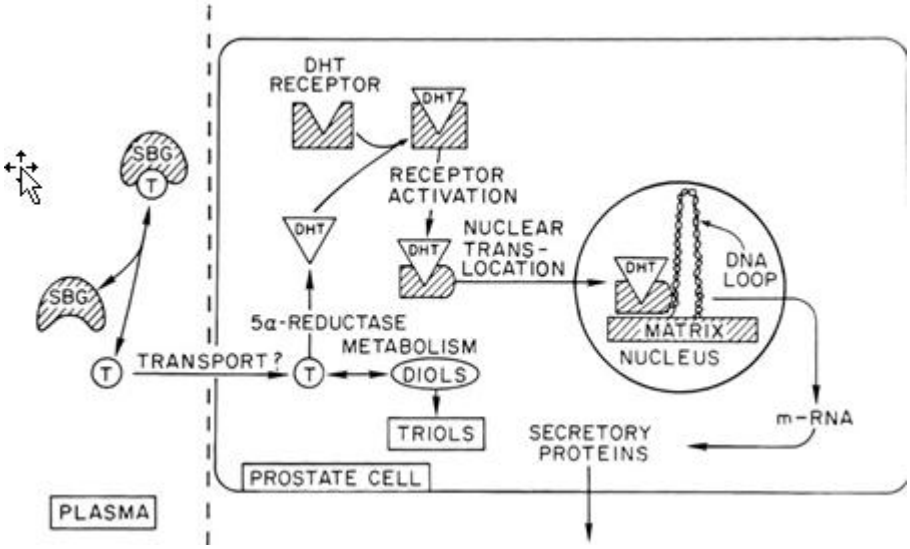


FIG. 2. Semi-diagrammatic representation of fibres of preprostatic sphincter passing round the urethra to interdigitate with the muscle fibres on the deep aspect of the striated muscle of the urethra.

Bladder Neck v Preprostatic Sphincter

Bladder Neck	Preprostatic sphincter
Both sexes	Males
At bladder neck	Supraverumontanal
Cholinergic innervation	Adrenergic innervation
Continence mechanism	Genital sphincter

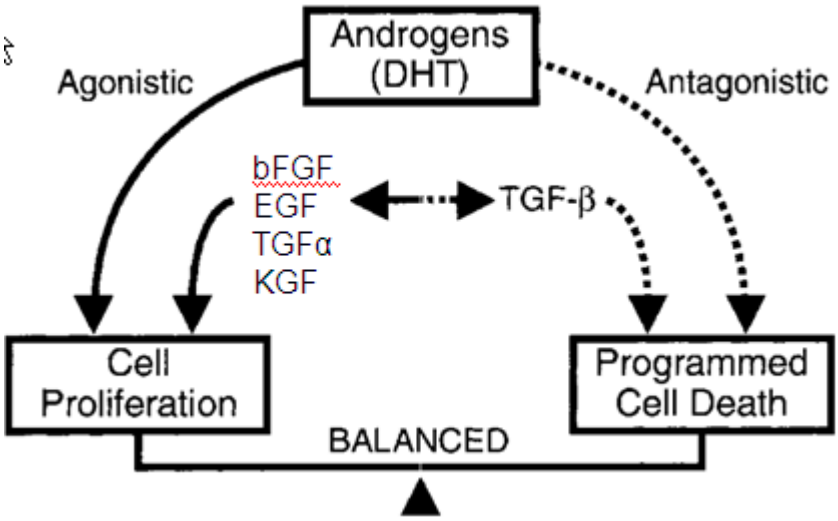
Endocrinology and physiology



Prostate function unknown - secretory
Testosterone required for normal function
Permissive role for growth; androgen withdrawal = prostate involution
Majority of serum testosterone from testis – unbound T bioavailable form
DHT formed within prostate epithelial cells – 40x more active vs. T
DHT diffuses to stroma (most of the androgen receptors; paracrine effect)
Stromal nuclei produce growth factors
Growth factors drive epithelial cells
Stimulatory
- bFGF, KGF (FGF-7) and EGF* and IGF (80%)
- TGFα (20%)

Inhibitory
- TGFβ

* EGF believed to be dominant factor regulating prostate epithelial growth



<u>Prostatic secretion</u>
Proteins and non-proteins (see below)
Zinc maintains quaternary structure of sperm chromatin

PSA aids liquefaction of seminal fluid
Citrate thought to act as buffer for seminal fluid (~750x conc. vs. other tissues)

Prostatic Secretion

Proteins	Non proteins
Acid phosphatase	Citrate
PSA	Spermine
Leucine aminopeptidase	Spermidine
Diamine oxidase	Putrescine
B Glucuronidase	Zinc
Plasminogen activator	Myoinositol
Complement C3 and C4	Cholesterol
Transferrin, transferritin	
Growth factors	
Annexin 1	